

## **REMARKS**

The Office Action dated November 19, 2003, has been received and reviewed. Claims 1-7, 9-11 and 14-16 are pending in the present application and stand rejected. Claim 8 stands withdrawn by the Examiner in view of the restriction requirement. Applicants respectfully request reconsideration of the application in view of the claim amendments above and the remarks below.

### **I. Specification Objections**

Applicants note that a new declaration will be filed in response to Office Action as soon as Applicants' representative receives the corrected declaration. Applicants submit that this will be filed as soon as possible. Applicants have also amended the title and abstract of the present application as suggested by the Examiner. Applicants have also included a sequence listing with the present response as well as amended the specification to include the sequence identification language. Accordingly, Applicants respectfully request that the objections to the specification be withdrawn.

### **II. Claim Amendments**

Claims 1, 3-9, 11, 14 and 16 have been amended to clarify the claim language in view of the claim objections and to correct for changes from European to United States patent practice. Claim 2 has been amended into independent form. Accordingly, Applicants respectfully submit that the claims are now in condition for allowance.

### **III. Claim Objections**

Claims 2-9, 11 and 14 are objected to as allegedly containing informalities. Applicants have amended claims 3-9, 11 and 14 to begin with the word "The" rather than "A". Applicants submit that every claim can stand alone, and note by changing the word "a" to "the" in no way changes the scope of the present claims. Applicants have also included comma as indicated in the areas suggested by the Examiner. Applicants have also amended Claim 2 into independent form to better claim the subject matter of original Claim 2. Accordingly, Applicants respectfully request that the objections to the claims be withdrawn in view of the amendments.

#### **IV. Rejections under 35 U.S.C. § 112, first paragraph**

##### A. Enablement

Claims 1-8, 10-11 and 14-16 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse these rejections due to the amendments to the claims and the reasons enumerated below.

Applicants note that the "test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (MPEP §2164.01, citing *In re Wands*, 858 F.2d 731, 737). Furthermore, the test for whether or not the enablement requirement has been met involves determining whether or not practice of the invention as claimed involves "undue experimentation". It has long been settled that "the key word is 'undue', not 'experimentation'". *In re Angstadt*, 190 USPQ 214, 219 (C.C.P.A. 1976). In the present case, the references cited by the Examiner in the previous Office Action, taken together with the references cited by the Applicants in this reply show only that the application of the current technology requires routine effort, and not undue experimentation.

Applicants submit that the present application discloses various methods that can be employed to achieve high BiP levels in plants. Specifically, page 5, line 19 to page 16, line 18 lays out methods for increasing BiP levels. Additionally, the Examples illustrate increased BiP levels. Furthermore, WO94/08012 published 14 April 1994, which was cited in the International Search report, illustrates enablement for means of over expression of BiP. WO94/08012 relates to the state of the art of methods of increasing secretory protein synthesis, especially by over-expressed gene product(s). Furthermore, Applicants submit that well-known techniques in the art of plant breeding can be utilized to positively select a plant for desired characteristics to achieve high BiP levels in plants. Therefore, Applicants submit that the Claims 1-8, 10-11 and 14-16 are enabled.

The Claims also stand rejected to as allegedly the specification fails to provide guidance for exact hybridization or amplification conditions other than those for encoding tobacco BiP. Applicants have enclosed as Appendix I a list of other nucleic acids listing various species and kingdoms encoding BiP that were known at the time of the invention. Among plants, BiPs are extremely conserved (over 90% sequence similarity at protein level), between kingdoms it is less (70%) as reported in Denecke et al., 1991 a document referred to in the specification on page 3 line 16, page 22 line 27, page 25 line 2 and page 26 line 2. However, as noted in the specification and by one of skill in the art, it will be appreciated that it is the protein sequence and not the nucleotide sequence which is important for determining function. Genes code for proteins but it is the proteins which act. Accordingly it is the homology at the protein level that is relevant and not at the nucleotide level. It has been observed that because of the degeneracy of the genetic code, two genes encoding exactly the same protein may have less than 50% sequence homology at the nucleotide level. The 1991 Denecke et al. reference illustrated that tobacco BiP can complement the yeast BiP (a conditionally lethal BiP mutant could be made viable by expressing tobacco BiP). This demonstrates that the function of BiP is extremely conserved, even between kingdoms of organisms, and is the basis for the claim that the present invention would work with any BiP from any eukaryotic cell, **not just** tobacco BiP. Applicants further submit that "BiP activity" could be measured by an assay as reported in Leborgne-Castel, 1999. Accordingly, Applicants submit that the present application is enabled. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, first paragraph to Claims 1-8, 10-11 and 14-16.

#### B. Written Description

Claims 1-7, 9-10 and 14-16 are also rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. Applicants respectfully disagree with this assertion.

Applicants note that the U.S.P.T.O. has clarified the standard for examining applications for compliance with respect to the written description requirement of 35 U.S.C. §112, first paragraph. These guidelines state, in part:

The examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed . . . . Consequently, rejection of an original claim for lack of written description should be rare.

(Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1105 (Jan. 5, 2001); emphasis added). Applicants respectfully contend that the specification does provide a sufficient written description so that one skilled in the art would appreciate that the Applicant was in possession of the claimed invention at the time of filing.

As noted above, Applicants have enclosed as Appendix 1, a list of other nucleic acids across species and kingdoms encoding BiP that were known at the time of the invention. The 1991 Denecke et al. reference cited to in the present application illustrates the highly conserved nature of BiP thus illustrating the broad range of nucleic acids that could be used in accordance with Claims 1-7, 9-10 and 14-16 of the present application. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, first paragraph to Claims 1-7, 9-10 and 14-16.

#### **V. Rejections under 35 U.S.C. § 112, second paragraph**

Claims 1-7, 9-11 and 14-16 are rejected under 35 U.S.C. §112, second paragraph for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, second paragraph rejections in view of the claim amendments and the following remarks.

Claim 1 stands rejected to as allegedly being indefinite. Applicants have amended Claim 1 to recite "maintaining" and removing reference to "causing". Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph to Claim 1.

Claims 1, 3-7, 10-11 and 14-16 stand rejected as allegedly being indefinite in their recitation of "homologue". Applicants note that on page 6 lines 11 to 12 it is stated: "For the purposes of this patent application the term BiP includes any homologue thereof which has a significant degree of structural or functional similarity". Accordingly, Applicants submit that the

term homologue is defined in the specification and therefore request that the rejections to Claims 1, 3-7, 10-11 and 14-16 be withdrawn.

Claims 5-7 stand rejected as it is allegedly unclear what the meaning of containing is. Applicants have amended containing to read comprising as suggested by the Examiner. Accordingly, Applicants submit that these claims are now in condition for allowance.

Claims 5-7 also stand rejected as allegedly being indefinite in their recitation of "3' untranslated end" and "stop sequence". Applicants have amended these claims to recite "3' untranslated region" and "stop codon". Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph to Claims 5-7.

Finally, Claim 16 stands rejected as allegedly being indefinite in its recitation of "in an amount sufficient to protect the plant". Applicants have added the recitations "in an amount sufficient to accelerate the induction of PR gene expression" to Claim 16. Support for this recitation can be found on page 18 lines 16 to 18. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112, second paragraph to Claim 16.

## **VI. Rejections under 35 U.S.C. § 102(b)**

### A. Crofts et al.

Claims 1-2 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Crofts et al., (1998) *Plant Cell* 10:813-823. Applicants respectfully traverse this rejection for the reasons set forth below.

Case law holds and the M.P.E.P. states that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Additionally, anticipation under 35 U.S.C. § 102 requires the disclosure in a single piece of prior art of each and every limitation of a claimed invention. *Apple Computer Inc. v. Articulate Systems Inc.* 57 USPQ2d 1057, 1061 (Fed. Cir. 2000).

Applicants note that prior to December 15, 1998, the earliest priority date of the present application, BiP or other ER chaperones are induced **during** plant pathogen **as a consequence** of high secretory protein synthesis. Again, prior to this date there was no disclosure that BiP over-

expression could **lead to resistance**, and BiP had never before been considered as a pathogenesis related protein (PR). The present application illustrates that BiP is induced **prior** to PR proteins. *See*, page 4 lines 6 to 16. The present application also illustrates that BiP over-expression leads to accelerated PR gene induction at the transcriptional level. Accordingly, this means the defense response is accelerated leading to the claims recited in the present application.

Applicants further note that one of the present inventors, Jurgen Denecke, is a co-author of the Crofts et al. citation, and note that this citation discloses plants transformed with a nucleic acid encoding BiP and plants overproducing calreticulin. However, Crofts et al. does not specifically disclose or teach plants with increased pathogen resistance. Instead, Crofts et al. on page 821 column 1 lines 5 to 8 states that “it is important to conduct further research to elucidate the function of this novel complex”. Thus, Crofts et al. merely identifies a complex, but is unable to provide a function for it such complex, because Crofts et al. it fails to appreciate the link between increased pathogen resistance and increased BiP levels. Accordingly, as recited in Claim 1, a method to increase secretory protein synthesis, and a method of reducing the period of time for responding to a pathogen attack in Claim 2 is not disclosed either explicitly or implicitly in the Crofts et al. Therefore, Applicants respectfully request reconsideration and withdrawal to the 35 U.S.C. § 102(b) rejections to Claims 1 and 2.

B. Arora et al.

Claims 1-4, 10-11 and 14-15 stand rejected as allegedly being anticipated by Arora et al. (1998) *Physiol. Planta.* 103: 24-34. Applicants respectfully disagree with this assertion. Applicants submit that Arora et al. discloses the observation that BiP accumulates in water stressed tissues of geranium plants and that tissue that is water stressed is more heat tolerant. There is no mention of a method of increasing secretory protein synthesis by causing a plant to maintain a level of BiP greater than the endogenous level under non-stressful conditions. Accordingly, independent Claims 1 and 2 and their subsequent dependent claims are not anticipated with respect to Arora et al. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 102(b) rejections to Claims 1-4, 10-11 and 14-15.

C. Zhang et al.

Claims 1-4, 10-11 and 14-15 also stand rejected as allegedly being anticipated by Zhang et al., (1992) *Protoplasma* 171: 142-152. Applicants respectfully disagree with this assertion. Applicants submit that Zhang et al. discloses maize mutant plants in which BiP levels are elevated. Zhang et al. Note that the elevation of BiP level is not thought to be as a result of a mutation in the BiP gene itself but rather as a result of stress. *See*, page 150, column 2, 2<sup>nd</sup> paragraph. Zhang et al. does not disclose a method to increase secretory protein synthesis nor a method of reducing the period of time for responding to a pathogen attack. Indeed, Zhang et al. is silent with respect to pathogens. Accordingly, Applicants submit that Claim 1-4, 10-11 and 14-15 are not anticipated by Zhang et al. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 102(b) rejections to Claims 1-4, 10-11 and 14-15.

**VII. Rejections under 35 U.S.C. § 103(a)**

A. Claims 1-7, 10-11 and 14-15

Claims 1-7, 10-11 and 14-15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Crofts et al., (1998) *Plant Cell* 10:813-823. Applicants traverse this rejection for the reasons set forth below and the reasons discussed above in the 102(b) section.

To establish a prima facie case of obviousness, the prior art reference or references when combined must teach or suggest *all* the recitations of the claim, and there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. § 2143. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. § 2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). To support combining references, evidence of a suggestion, teaching, or motivation to combine must be clear and particular, and this requirement for clear and particular evidence is not met by broad and conclusory statements about the teachings of references. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Court of Appeals for the Federal Circuit has also stated that, to support combining or modifying references, there must be particular evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55

U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000). Furthermore, as recently affirmed by the Court of Appeals for the Federal Circuit in *In re Sang-su Lee*, a factual question of motivation is material to patentability, **and cannot be resolved on subjective belief and unknown authority**. See *In re Sang-su Lee*, 277 F.3d 1338 (Fed. Cir. 2002). Respectfully, as will be discussed below, the Official Action fails to meet the requirements for a prima facie showing of obviousness under § 103.

Applicants re-emphasize that BiP acts as a "trigger" to accelerate pathogen resistance and not merely as a consequence of a pathogen challenge. This is corroborated by the data in Figures 11 and 12 and in Examples 12 and 13 of the application. Applicants submit that Crofts et al. does not teach or suggest the constructs used to transform the plants and the levels of BiP produced in the present invention. The methods disclosed by Crofts et al. refer to a method by N. Leborgne-Castel and J. Denecke for teaching transgenic plant that overexpress BiP. See, *Plant Cell*, (1999) 11(3): 459-70. The N. Leborgne-Castel and J. Denecke paper was not published until March 1999, i.e., after the earliest priority date of the present application. Therefore, not only is Crofts et al. not enabling, but there is no suggestion or motivation to modify the teachings of Croft et al. to arrive at the present invention as claimed in Claims 1-7, 10-11 and 14-15. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejections to Claims 1-7, 10-11 and 14-15.

#### B. Claims 9 and 16

Claims 9 and 16 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Crofts et al. in combination with Denecke et al. (1995) *Plant Cell* 7: 391-406. Applicants respectfully disagree with this assertion. Applicants note that it is alleged that Denecke et al. teaches that levels of BiP are increased in **response** to salicylic acid, and that one of ordinary skill in the art would have been motivated to increase the expression of BiP in plants with SA. However, as previously mentioned Crofts et al. is not enabling for the present claims and there is no motivation to combine Crofts et al. with Denecke et al. because Crofts et al. is concerned with the function of the BiP-calreticulin complex and not pathogen resistance. Applicants submit that the combination of these documents would not lead to Claims 9 and 16 as one of ordinary skill in the art would not have been able to develop plant resistance by a mere combination of these documents. As in *In re Sang-su Lee*, a factual question of motivation is material to patentability,



and cannot be resolved on subjective belief and unknown authority. Accordingly, Applicants submit that the combination of Crofts et al. and Denecke et al. does not teach or suggest the elements of Claims 9 and 16 of the present application.

C. Claims 1-4, 6, 10, 11, 14 and 15

Claims 1-4, 6, 10, 11, 14 and 15 also stand rejected as allegedly being unpatentable in view of Coughlan et al., U.S. Patent No. 6,171,864. Applicants respectfully disagree with this assertion. The '864 patent discloses novel compositions for calreticulin and calnexin proteins, genomic sequences, and promoters as well as uses of these proteins and sequences in controlling expression of resistance genes. It further discloses plant cells transformed with a vector encoding calreticulin, which it is believed would increase the levels of BiP in the plant over endogenous levels. However, the '864 patent merely acknowledges that BiP is one of an array of chaperones and does not disclose plants transformed with a vector encoding calreticulin. Applicants submit that there is no suggestion or motivation to modify the teachings of this reference or to combine it with any other citation to the presently claimed methods of increasing secretory protein synthesis or reducing the period of time for responding to a pathogen attack. Accordingly, Applicants submit that the '864 patent does not teach or suggest all of the elements of Claims 1-4, 6, 10, 11, 14 and 15. Therefore, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejections to Claims 1-4, 6, 10, 11, 14 and 15.

**CONCLUSION**

In view of the remarks presented herein, Applicants respectfully submit that the claims define patentable subject matter. If, in the opinion of the Examiner, a telephonic conference would expedite the examination of this matter, the Examiner is invited to call the undersigned attorney at (919) 854-1400.

Applicants have included a one-month extension of time fee with this response. It is believe that no other fees and/or additional fee(s)-including fees for net addition of claims-are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that an extension of time is necessary to allow consideration of this paper, such an extension is hereby petitioned under 37 C.F.R. §1.136(a). Any additional fees

In re: Denecke et al.  
Serial No.: 09/868,434  
Filed: June 15, 2001  
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believed to be due in connection with this paper may be charged to our Deposit Account No. 50-0220.

Respectfully Submitted,



Jarett K. Abramson  
Registration No. 47,376

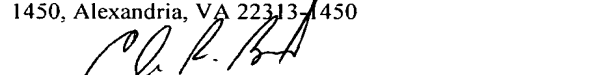
**USPTO Customer No.: 20792**  
Myers Bigel Sibley & Sajovec, P.A.  
Post Office Box 37428  
Raleigh, NC 27627  
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Facsimile (919) 854-1401

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Date of Deposit: March 19, 2004

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Clara R. Beard

## Appendix . I

### Non-plant BiPs published before filing in December 1998

#### *Saccharomyces cerevisiae* (Yeast)

Rose MD, Misra LM, Vogel JP.

KAR2, a karyogamy gene, is the yeast homolog of the mammalian BiP/GRP78 gene. Cell. 1989 Jun 30;57(7):1211-21.

mffnrlsagk llvplsvvly alfvvilplq nsfhssnvlv

41 rgaddvenyg tvigidlgtt yscvavmkng kteilaneqg  
81 nritpsyvaf tdderligda aknqvaanpq ntifdikrli  
121 glkyndrsdq kdikhlpfnv vnkdgkpave vsvkgekkvf  
161 tpeesgmil gkmkqiaedy lgtkvthavv tpayfndaq  
201 rqtatkdagi aglnvlrvn eptaaaiayg ldksdkehqi  
241 ivydlgggtf dvslisieng vfevqatsgd thlggedfdy  
281 kivrqlikaf kkkhgidvds nnkalaklr eakakrals  
321 sqmstrieid sfvdgidlse tltrakfeel nldlfktilk  
361 pvekvldsg lekdvddiv lvggstripk vqqllesyfd  
401 gkkaskginp deavaygaav qagvlsgeeg vedivlldvn  
441 altlgieltg gvmtplikrn taiptrksqi fstavdnqpt  
481 vmikvyeger amskdnllg kfeltgippa prgvpqievt  
521 faldangilk vsatdkgtgk sesitindk grltqeeidr  
561 mveeaekfas edasikakve smklenyah slknqvngdl  
601 gekleedke tlldaandvl ewlddnfeta iaedfdekfe  
641 slskvaypit sklyggadgs gaadyddede dddgdyfeh  
681 el

#### *Aspergillus* (mold)

Hijarrubia, M. J., Casqueiro, J., Gutierrez, S., Fernandez, F. J., and Martin, J. F.

Characterization of the bip gene of *Aspergillus awamori* encoding a protein with an HDEL retention signal homologous to the mammalian BiP involved in polypeptide secretion.

Curr Genet 32, 139-46 (1997).

marishqgaa kpftawttif ylllvfiapl affgtahaqd

41 etspqesygt vigidlgtty scvgvmqngk veilvndqgn  
81 ritpsyvaft deerlvgdad knqyaanprn tiftikrlig  
121 rkfdkdvqk dakhfpykvv nkdgkphkv dvnqtpklt  
161 peevsamvlg kmkeiaegyl gkkvthavvt vpayfndaqr  
201 qatkdagtia glnlrvvne ptaaaiaagl dktgderqvi  
241 vydlgggtfd vsllsidngv fevlatagdt hlgedfdqr  
281 vmdhfvklyn kknvndvtdk lkamgklkre vekakrtlss  
321 qmstrieiea fhngedfset ltrakfeeln mldlfktilkp  
361 veqvlkdakv kksevddivl vggstripkv qalleeffgg  
401 kkaskginpd eavafgaavq ggvlsggegt gdvvlmdvnp  
441 ltgielttg vmtkliprnt viptrksqi staadnqptv  
481 liqvyegers ltkdnllgk feltgippa rgvpqievsv  
521 dldangilkv hasdkgtgka esitindkg rlsqeedrm  
561 vaeaeefae dkaikakiea mtlenyafs lknqvndeng  
601 lggqideddk qtildavkev tewlednaat attedfeeck  
641 eqlsnvaypi tsklygsapa deddepsghd el



### **Nematode worm**

Wilson,R.

Genome sequence of the nematode *C. elegans*: a platform for investigating biology. The *C. elegans* Sequencing Consortium  
JOURNAL Science 282 (5396), 2012-2018 (1998)

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mktlflgli alsavsvyce eeektekket kygtiigidl gttyscvgy kngrveiiian
 61 dqgnritpsy vafsgdqgdr ligdaaknql tinpentifd akrigrdyn dktvqadikh
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181 fndaqrqatk dagtiaglnv vriineptaa aiaygldkkd gernilvfdl gggtfdvsml
241 tidngvfevl atngdthlgg edfdqrmey fiklykkksk kdlrkdkrav qklrreveka
301 kralstqhqt kveieslfdg edfsetltra kfeelnmdlf ratlkpvqkv ledsdlkkdd
361 vheivlvggs tripkvqqli keffngkeps rginpdeava ygaavqggvi sgeedtgeiv
421 lldvnpltmg ietvvgvmtk ligntvtipt kksqvfstaa dnqptvtiqv fegerpmtkd
481 nhqlgkfdlt glppaprgvp qievtfeidv ngilhvtad kgtgnknkit imdqnrslp
541 edierminda ekfaeddkkv kdkaeamel esaynlknq iedkeklggk ldeddkkie
601 eaveeaiswl gsnaeasae lkeqkkdles kvqipvskly kdagaggeea peegsddkde
661 l
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### **Chicken**

Stoeckle,M.Y., Sugano,S., Hampe,A., Vashistha,A., Pellman,D. and Hanafusa,H.

78-kilodalton glucose-regulated protein is induced in Rous sarcoma virus-transformed cells independently of glucose deprivation  
Mol. Cell. Biol. 8 (7), 2675-2680 (1988)

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1 mrhlallll lgaraddee kkedvgtvvg idlgttyscv gvfkngrvei iandqgnrit
 61 psyvaftpeg erligdaakn qltsnpentv fdakrligt wndpsvqqdi kylpflkvvek
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361 ggstripkiq qlvkeffngk epsrginpde avaygaavqa gvlsgdqdtdg dlvlldvcpl
421 tlgietyggv mtklipmtv vptkksqifs tasdnqptvt ikvyegerpl tkdnhlgtf
481 dltgippapr gvpqievtfe idvngilrvt aedkgtgnkn kititndqnr ltpееiervv
541 ndaekfaeed kklkeridar nelesyaysl knqigdkekl ggklssedke tiekaveeki
601 ewleshqdad iedfkskkke leevvqpivs klygsagppp tgeeeaaekd el
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### **Chinese Hamster**

Ting,J., Wooden,S.K., Kriz,R., Kelleher,K., Kaufman,R.J. and Lee,A.S.

The nucleotide sequence encoding the hamster 78-kDa glucose-regulated protein (GRP78) and its conservation between hamster and rat

Gene 55 (1), 147-152 (1987)

```
1 mkfpmvaaal llcavraee edkkedvgtv vgidlgttys cvgvfkngrv eiiandqgnr
 61 itpsyvaft egerligdaa knqltsnpen tvfdakrlig rtwndpsvqq dikflpflvv
121 ekktkpyiqv digggqtktf apeesamvl tkmketaeay lgkkvtavv tvpayfndaq
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 601 kiewleshqd adiedfkakk keleeivqpi isklygsagp pptgeedtse kdel

#### Mouse

Kozutsumi, Y., Normington, K., Press, E., Slaughter, C., Sambrook, J.  
 and Gething, M. J.

Identification of immunoglobulin heavy chain binding protein as  
 glucose-regulated protein 78 on the basis of amino acid sequence,  
 immunological cross-reactivity, and functional activity  
 J. Cell Sci. Suppl. 11, 115-137 (1989)

mmkftvvaaa llllgavrae eedkkedvgt vvgidlgty scvgvfkngr veiiandqgn  
 61 ritpsyvaft pegerligda aknqltsnpe ntvfdakrli grtwnbpsvq qdikflpfkv  
 121 vekktkpyiq vdigggqtkf fapeeisamv ltkmketaea ylgkkvthav vtvpayfnda  
 181 qrqatkdaqt iaglnvmrii neptaaaiay gldkregekn ilvfdlgggt fdvsltidn  
 241 gvfevvatng dthlggedfd qrvmehfikl ykkktgkdvr kdnravqklr revekakral  
 301 ssqhqariei esffegedfs etltrakfee lnmldfrstm kpqkvleds dlkksdidei  
 361 vlvggstrip kiqqlvkeff ngkepsrgin pdeavayga vqagvlsdgd dtgdlvldv  
 421 cpltlgiety ggvmtnklipr ntvpstkksq ifstasdnqpt vtikvyeger pltkdnhll  
 481 gtfdltgippa prgvpqievt feidvngilr vtaedkgtg nknkititnd qnrltpeeie  
 541 rmvndaekfa eedkklkeri dtmelesya yslknqigdke eklggklssed dketmekave  
 601 ekiewleshq dadiedfkak kkeleeivqp iisklysgg ppptgeedts ekdel

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#### A selection of plant BiP sequences published before filing in December 1998

Tobacco BiP in 1991, you have this references and it cites 8 isoforms of tobacco BiP,  
 which could mean that there are 8 or more isoforms in tobacco. The patent is based on  
 isoform 4 (BLP4), but the other isoforms are over 90% identical

#### Arabidopsis thaliana

Koizumi, N.

Isolation and responses to stress of a gene that encodes a luminal binding protein in  
 Arabidopsis thaliana

Plant Cell Physiol. 1996

Volume 37

862-865

#### Soybean

Figueiredo, J.E.F., Cascardo, J.M., Carolino, S.M.B., Alvin, F. and  
 Fontes, E.P.B.

Water-stress regulation and molecular analysis of the soybean BIP

gene family

Braz. J. Plant Physiol. 9, 103-110 (1997)

#### **Rice**

Muench,D.G., Wu,Y., Zhang,Y., Li,X., Boston,R.S. and Okita,T.W.

Molecular cloning, expression and subcellular localization of a BiP homolog from rice endosperm tissue

Plant Cell Physiol. 38 (4), 404-412 (1997)

#### **Maize**

Wrobel,R.L., OBrian,G.R. and Boston,R.S.

Comparative analysis of BiP gene expression in maize endosperm

Gene 204 (1-2), 105-113 (1997)

#### **Spinach**

Anderson,J.V., Neven,L.G., Li,Q.B., Haskell,D.W. and Guy,C.L.

A cDNA encoding the endoplasmic reticulum-luminal heat-shock protein from spinach (*Spinacia oleracea* L.)

Plant Physiol. 104 (1), 303-304 (1994)

#### **Tobacco BLP4 (one of 8 cloned isoforms, there could be more than 8)**

maggawnrrt slivfgivlf gclfafsiat eatklgtvi gidlgttysc vgvyknghve

61 iiaandqgnri tpswvaftdg erligeaakn laavnpertv fdvkrigrk fddkevqrđm

121 klvpykivnk dgkpyiqvki kdgetkifsp eeisamiltk mketaeaylg kkikdavvtv

181 payfindaqrq atkdagviag lnvariinep taaaiaaygld kkggekniltv fdlgggtfdv

241 siltidngvf evlstngdth lggedfdqri meyfikkikk khgkdiskdn ralglrrea

301 erakralssq hqvrveiesl fdgvdfsepl trarfeelnn dlfiktngpv kkamddagle

361 ktqideivlv ggstripkvq qlldkdyfdgk epnkgvnpde avaygaavqg gilsgeggde

421 tkdillldva pltlgietyg gvmtklipm tviptkksqv ftyqdqqt vtiqvfege

481 sltkdcrllg kfdltgiapa prgtpqievt fevdangiln vkaedkasgk sekititndk

541 grlsqeeier mvkeaeefae edkkvkerid amsletyvy nmrnqindkd kladklesde

601 kekietatke alewlđdnqs aekedyekl keveavcnpi itavyqksgg apggesgase

661 dđđhđel

#### **Arabidopsis thaliana (one of three isoforms in this species)**

marsfganst vvlaiiffgc lfafstakee atklgsvigi dlgttyscvg vykngheii

61 andqgnritp swvgftdser ligeaaknqa avnpertvfd vkrigrkfe dkevqkdrkl

121 vpyqivnkdg kpyiqvikid getkvfspee isamiltkmk etaeaylgkk ikdavvtvpa

181 yfindaqrqat kdagviagln variinepta aaiaygldkk ggekniltvfd lgggtfdvsv

241 ltidngvfev lstngdthlg gedfdhrime yfiklikkkh qkdiskdnka lgklrrecer

301 akralsqhq vrveieslfd gvdlseplr arfeelnnđl frktmgpvkk amddaglkqs

361 qideivlvvgg stripkvqql lkdfefegkep nkgvnpdeav aygaavqggi lsgeggdetk

421 dillldvaplt lgietyggv mtklipmtv iptkksqvft tyqdqqtvs iqvfegersl

481 tkdcsllgkf dltgvppapr gtpqievtfe vdangilnvk aedkasgkse kititnekgr

541 lsqeeidrmv keaeefaeed kkvkekidar naletyvynm knqvsdkdkl adklegdeke

601 kieaatkeal ewldenqnse keeydeklke veavcnpiit avyqrsaggap gaggesstee

661 edeshđel

### Glycine max

magswarrsl ivlaiisfgc lfaisiakee atklgtvigi dlttyscvg vykngheii

61 annqgnritp swvaftdser ligeaaknla avnpertifd vkrigrkfe dkevqrdmkl  
121 vpykivnkdg kpyiqvkikd getkvfspee isamiltkmk etaeafgkk indavvtvpa  
181 yfndaqrqat kdagviagln variinepta aaiaygldkk ggeknilvfd lgggtfdvsi  
241 ltidngvfev latngdthlg gedfgqrime yfiklikkkh gkdiskdnra lgklrreaer  
301 akralsqbq vrveieslfd gvdsepltr arfeelnndl frktmgpvkk amedaglqks  
361 qideivlvvg stripkvqql lkdyfdgkep nkgvnpdeav aygaavqegi lsgeggeetk  
421 diilldvapl tlgienvvgv mtklipmtv iptkksqvft tyqdqqtvs iqvfegersl  
481 tkdcrllgkf dlsgippapr gtaqievtfe vdangilnvk aedkgtgkse kititnekgr  
541 lsqeeierv reekdfaeee kvkeridar nsletyvynm knqvsdkdkl adklesdeke  
601 kietavkeal ewlddnqsm kedyeeikle veavcnpiis avyqrsggap ggggasgeed  
661 eddshdel

### Rice

mdrvrgsafl lgvllagslf afsvakeetk klgtvigidl gttyscvgvy knghveiian

61 dqgnritpsw vaftdserli geaaknqaav npertifdvk rdigrkfeek evqrdmklvp  
121 ykivnkigkp yiqvkikdge nkvspeevs amilgkmmk etaylgkkin davvtvpayf  
181 ndaqrqatkd agviaglnva riineptaaa iaygldkkkg eknilvfdlg ggtfdvsilt  
241 idngvfevla tngdthlgge dfdqrimyef iklikkkysk diskdnralg klrreaerak  
301 ralsnqhqr veieslfdgt dfsepltrar feelnndlfr ktmgvpvkkam ddagleksqi  
361 heivlvvgst ripkvqqlr dyfegkepknk gvpndeavay gaavqgsils geggdetkdi  
421 lldvapltil gietvggvmv klipmtvip tkksqvftty qdqqttsiq vfegersmtk  
481 dcrllgkfdl sgipaaprgt pqievtfevd angilnvkae dkgtgkseki titnekgrls  
541 qeeidrmv reeafaedkk vkeridamq letyvynmkn tvgdkdklad kleseekekv  
601 eealkealew ldenqtaeke eyeekkeve avcnpiisav yqrtggapgg rrrgrlddeh  
661 del

### Maize

mdrvrgsafl lgvllagslf afsvakeetk klgtvigidl gttyscvgvy knghveiian

61 dqgnritpsw vaftdserli geaaknqaav npertifdvk rligrkfkd evqrdmklvp  
121 ykiinkdgkp yiqvkikdge nkvspeeis amilgkmmk etaylgkkin davvtvpayf  
181 ndaqrqatkd agviaglnva riineptaaa iaygldkkkg eknilvfdlg ggtfdvsilt  
241 idngvfevla tngdthlgge dfdqrimyef iklikkkysk diskdnralg klrreaerak  
301 ralsnqhqr veieslfdgt dfsepltrar feelnndlfr ktmgvpvkkam edagleksqi  
361 heivlvvgst ripkvqqlr dyfngkepknk gvpndeavaf gaavqgsils geggdetkdi  
421 lldvapltil gietvggvmv klipmtvip tkksqvftty qdqqttsiq vfegersmtk  
481 dcrllgkfdl ngipsaprgt pqievtfevd angilnvkae dkgtgkseki titnekgrls  
541 qeeidrmv reeafaedkk vkeridamq letyvynmkn tvgdkdklad kleaeekkv  
601 eealkealew lddnqsaeke dyeekkeve avcnpiisav yqrsggapgg dadggvdddh  
661 del

### Spinach

mavawksras siafgivllg slfafvsakd eapklgtvig idlttyscv gvykdgkvei

61 iandqgnrit pswwaftnde rligeaaknq aanpertif dvkrigrkf edkevqkdmk  
121 lvpykivnrd gkpyiqkvq egetkvfspe eisamiltkm ketaetflg kikdavvtvp

181 ayfndaqrqa tkdagviagl nvariinept aaaiaygldk rggeknilvf dlgggtfdvs  
241 vltidngvfe vlatngdthl ggedfdqrlm eyfiklikkk htkdiskdnr algklrrece  
301 rakralssqh qvrveieslf dgvdseplf rarfeelnnd lfrktmgpvk kamddaglek  
361 nqideivlvq gstripkvqq llkeffngke pskgvnpdea vafgaavqgs ilsgeggeet  
421 keillldvap ltlgietvgg vmtkliprnt viptkksqvf ttyqdqqtiv tiqvfevers  
481 ltkdcrlgk fdlgtiapap rgtpqievtf evdangilnv kaedkasgks ekititndkg  
541 rlsqeeierm vreaeefae dkkvkekida msletyyn mknqisdadk ladklesdek  
601 ekiegavkea lewlddnqsa ekedydeklk eveavcnpii tavyqrsggp sgesgadsed  
661 seeghdel